# General

## Guideline Title

Proton beam radiation therapy.

## Bibliographic Source(s)

Proton Therapy Guideline Working Group, Guideline Advisory Group. Proton beam radiation therapy. Edmonton (AB): Alberta Health Services, Cancer Care; 2013 Mar. 20 p. (Clinical practice guideline; no. RT-002). [86 references]

## Guideline Status

This is the current release of the guideline.

# Recommendations

## Major Recommendations

1. A wide range of factors must be taken into account in assessing if proton beam radiotherapy will confer a significant advantage for the patient over standard conformal or stereotactic radiotherapy available in Alberta – the diagnosis alone is not sufficient.
2. Pediatric and adolescent tumour sites that may be considered for referral for out-of-country proton beam radiotherapy include:
    a. Those requiring craniospinal irradiation
    b. The following central nervous system (CNS) tumours or lesions: arteriovenous malformations, ependymomas, craniopharyngiomas, CNS germ cell tumours, primitive neuroectodermal tumours, and low grade gliomas
    c. The following non-CNS tumours: sarcomas including chordoma and chondrosarcoma, rhabdomyosarcoma, Ewing's sarcoma, pineal tumours, and lymphoma.
3. Adult tumour sites that may be considered for referral for out-of-country proton beam radiotherapy include:
    a. The following CNS tumours or lesions: arteriovenous malformations, benign meningioma, neuromas, craniopharyngioma, CNS germ cell tumours, and low grade gliomas
    b. The following non-CNS tumours: sarcoma including chordoma and chondrosarcoma, lymphoma in patients under the age of 30 years, and paranasal sinus and nasal cavity tumours.
4. Adult, pediatric, and adolescent patients with ocular melanomas requiring proton beam radiotherapy should be sent to the TRIUMF Proton Treatment Facility in Vancouver, British Columbia (BC) for treatment.
5. Members of the working group do not currently recommend that patients with prostate cancer, non-small cell lung cancer, or most lymphomas be referred for proton beam radiotherapy, due to an insufficient evidence base. However, individual patient cases should be discussed by the multidisciplinary team during a Tumour Board meeting.
6. For adult, adolescent, and pediatric cases, the referral for proton beam radiotherapy must come from the consultant oncologist who has seen and assessed the patient. Before the referral is made, a full multidisciplinary Tumour Board meeting should be held in which all tumour group members, including a radiation oncologist, have the opportunity to provide input on the case. In cases of arteriovenous malformations

in which there is no tumour present, discussion at an appropriate multidisciplinary meeting that includes a radiation oncologist should follow the same processes as described for multidisciplinary Tumour Board meetings.

7. Approval of the referral must be submitted to the Out-of-Country Health Services Committee, which operates at arm's length from Alberta Health. Once approved, the responsibility for referral and communications with the proton beam therapy treatment centre remains with the referring oncologist. The responsibility for follow-up and continuity of care also rests with the referring oncologist.
8. Additional and over-riding principles for approval and funding include:
    a. The treatment should be given with curative intent
    b. The patient should have a good performance status (0-2)
    c. The expected survival of the patient should be greater than 5 years
    d. The patient must be able and willing to travel

## Clinical Algorithm(s)

None provided

# Scope

## Disease/Condition(s)

- Central nervous system (CNS) tumours or lesions: arteriovenous malformations, ependymomas, craniopharyngiomas, CNS germ cell tumours, primitive neuroectodermal tumours, and low grade gliomas, benign meningioma, and neuromas
- Non-CNS tumours: sarcomas including chordoma and chondrosarcoma, rhabdomyosarcoma, Ewing's sarcoma, pineal tumours, lymphoma, and paranasal sinus and nasal cavity tumours

## Guideline Category

Management

Treatment

## Clinical Specialty

Neurological Surgery

Oncology

Pediatrics

Radiation Oncology

## Intended Users

Advanced Practice Nurses

Nurses

Physician Assistants

Physicians

## Guideline Objective(s)

- To evaluate the most current evidence for the use of proton beam radiotherapy in pediatric and adult patients with cancer, and to develop a de novo guideline with recommendations based on an expert review of the available literature
- To establish a process to identify which patients are appropriate candidates to receive out-of-country treatment with proton beam radiation therapy

## Target Population

Pediatric, adolescent, and adult patients who are residents of Alberta and may qualify to receive proton beam radiotherapy at a facility outside of Canada for treatment of their cancer

## Interventions and Practices Considered

1. Identification and election of patients likely to benefit from proton beam radiation therapy
2. Referral and funding process for out-of-country treatment

## Major Outcomes Considered

- Acute and long-term toxicities, including radiation-induced second malignancies
- Patient outcomes including rates of local control, progression-free survival, and overall survival
- Recurrence rates

# Methodology

## Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

## Description of Methods Used to Collect/Select the Evidence

Guideline Questions

- What is the evidence for the use of proton beam radiation therapy for the management of patients with cancer?
- What are the published recommendations for the selection of patients most likely to benefit from treatment with proton beam radiation therapy?
- What are the steps involved in referring a patient for out-of-country proton beam radiation therapy?

Search Strategy

Medical journals were searched using the MEDLINE (1950 to April Week 4, 2012), EMBASE (1980 to April Week 4, 2012), Cochrane Database of Systematic Reviews (1st Quarter, 2012), Cochrane Central Register of Controlled Trials (1st Quarter, 2012), and PubMed electronic databases; the references and bibliographies of studies identified through these searches were scanned for additional sources. The MEDLINE search terms were: Protons (MeSH term) OR Radiotherapy, High Energy (MeSH term) OR particle beam therapy OR charged particle therapy AND Skull Base Neoplasms (MeSH term) OR Spinal Neoplasms (MeSH term) OR Chondrosarcoma (MeSH term) OR Chordoma (MeSH term) OR Sarcoma (MeSH term). The search was limited to studies published in the English language between the years 2000 and 2012. There were no limitations by study design. A search for new or updated guidelines, health technology assessments, and medical policies was conducted by accessing the websites of guideline developers and the National Guideline Clearinghouse database, and by searching the grey literature using online search engines. Summaries of published clinical practice guideline recommendations and health technology assessments are available in Appendix A in the original guideline document.

## Number of Source Documents

Not stated

## Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

## Rating Scheme for the Strength of the Evidence

Not applicable

## Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

## Description of the Methods Used to Analyze the Evidence

The Alberta Health Services Cancer Care Proton Therapy Guideline Advisory Group members individually reviewed the results of an environmental scan and literature review conducted by a Knowledge Management (KM) Specialist from the Guideline Utilization Resource Unit (GURU). Members of this group include representatives from Alberta Health, as well as the departments of medical oncology, radiation oncology, and pediatric neurosurgery at the two tertiary cancer centres in Alberta. A detailed description of the methodology followed during the guideline development process can be found in the Guideline Utilization Resource Unit Handbook (see the "Availability of Companion Documents" field).

Evidence Tables

Evidence tables containing the first author, year of publication, patient group/stage of disease, methodology, and main outcomes of interest are assembled using the studies identified in the literature search. Existing guidelines on the topic are assessed by the KM Specialist using portions of the Appraisal of Guidelines Research and Evaluation (AGREE) II instrument (http://www.agreetrust.org) and those meeting the minimum requirements are included in the evidence document. Due to limited resources, GURU does not regularly employ the use of multiple reviewers to rank the level of evidence; rather, the methodology portion of the evidence table contains the pertinent information required for the reader to judge for himself the quality of the studies.

## Methods Used to Formulate the Recommendations

Expert Consensus

## Description of Methods Used to Formulate the Recommendations

Formulating Recommendations

The working group members formulated the guideline recommendations based on the evidence synthesized by the Knowledge Management (KM) Specialist during the planning process, blended with expert clinical interpretation of the evidence. As detailed in the Guideline Utilization Resource Unit Handbook (see the "Availability of Companion Documents" field), the working group members may decide to adopt the recommendations of another institution without any revisions, adapt the recommendations of another institution or institutions to better reflect local practices, or develop their own set of recommendations by adapting some, but not all, recommendations from different guidelines.

The degree to which a recommendation is based on expert opinion of the working group and/or the Provincial Tumour Team members is explicitly stated in the guideline recommendations. Similar to the American Society of Clinical Oncology (ASCO) methodology for formulating guideline recommendations, the Guideline Utilization Resource Unit (GURU) does not use formal rating schemes for describing the strength of the recommendations, but rather describes, in conventional and explicit language, the type and quality of the research and existing guidelines that were

taken into consideration when formulating the recommendations.

### Rating Scheme for the Strength of the Recommendations

Not applicable

### Cost Analysis

In a modeling study evaluating the consequences of radiotherapy in five-year-old patients with medulloblastoma, researchers reported that proton radiation therapy was cost-effective and was associated with an additional 0.68 quality-adjusted life-years per patient compared with conventional photon radiotherapy. Reductions in IQ loss and growth hormone deficiency contributed most to the cost savings and were the most important parameters for cost-effectiveness. This analysis suggests that proton beam radiotherapy may be cost-saving in comparison to photon radiotherapy for pediatric patients with medulloblastoma due to the reduction of late side-effects. A reduction in side-effects for pediatric patients with medulloblastoma treated with proton beam radiotherapy was also recently demonstrated in a prospective study of 23 pediatric patients who were followed for high-grade ototoxicity, although a cost-benefit analysis was not reported for this trial.

A formal analysis was not conducted by the authors to evaluate the cost of referring a patient for out-of-country proton beam radiation therapy.

### Method of Guideline Validation

External Peer Review

Internal Peer Review

### Description of Method of Guideline Validation

The Guideline Working Group distributed a draft document via an anonymous electronic survey to 17 healthcare professionals from various disciplines within the province for review and comment. The response rate was 59%. The comments from the external review were incorporated into the guideline draft by the Guideline Working Group.

The final guideline was reviewed and endorsed in February 2013 by the Alberta Health Services Cancer Care Proton Therapy Guideline Advisory Group and Guideline Working Group, and was posted on the external website in March 2013.

## Evidence Supporting the Recommendations

### Type of Evidence Supporting the Recommendations

The recommendations are supported by prospective or retrospective case series, cohort studies, and clinical practice guidelines.

## Benefits/Harms of Implementing the Guideline Recommendations

### Potential Benefits

- Accurate identification of patients who are appropriate candidates to receive out-of-country treatment with proton beam radiation therapy
- Compared with conventional photon radiotherapy, proton beam therapy is associated with a reduction in acute and long-term toxicities, as well as lower rates of radiation-induced second malignancies, and potentially less acute and long-term damage to developing organs in pediatric and adolescent patients with cancer.
- Improved patient outcomes including improved rates of local control, progression free survival, and overall survival

### Potential Harms

Radiation-induced side effects

## Qualifying Statements

### Qualifying Statements

The recommendations contained in this guideline are a consensus of the Alberta Health Services Cancer Care Proton Therapy Guideline Working Group and Guideline Advisory Group synthesis of currently accepted approaches to management, derived from a review of relevant scientific literature. Clinicians applying these guidelines should, in consultation with the patient, use independent medical judgment in the context of individual clinical circumstances to direct care.

## Implementation of the Guideline

### Description of Implementation Strategy

- Present the guideline at relevant local and provincial tumour team meetings and weekly rounds.
- Post the guideline on the Alberta Health Services website as well as the Alberta Health website.
- Send an electronic notification of the new guideline to all members of Alberta Health Services, Cancer Care.

### Implementation Tools

Chart Documentation/Checklists/Forms

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

## Institute of Medicine (IOM) National Healthcare Quality Report Categories

### IOM Care Need

Getting Better

Living with Illness

### IOM Domain

Effectiveness

## Identifying Information and Availability

### Bibliographic Source(s)

Proton Therapy Guideline Working Group, Guideline Advisory Group. Proton beam radiation therapy. Edmonton (AB): Alberta Health

Services, Cancer Care; 2013 Mar. 20 p. (Clinical practice guideline; no. RT-002). [86 references]

## Adaptation

Not applicable: The guideline was not adapted from another source.

## Date Released

2013 Mar

## Guideline Developer(s)

CancerControl Alberta - State/Local Government Agency [Non-U.S.]

## Source(s) of Funding

Alberta Health Services, Cancer Care

## Guideline Committee

Alberta Health Services Cancer Care Proton Therapy Guideline Advisory Group

## Composition of Group That Authored the Guideline

Not stated

## Financial Disclosures/Conflicts of Interest

Participation of members of the Alberta Health Services Cancer Care Proton Therapy Guideline Working Group and Guideline Advisory Group in the development of this guideline has been voluntary and the authors have not been remunerated for their contributions. There was no direct industry involvement in the development or dissemination of this guideline. Alberta Health Services Cancer Care recognizes that although industry support of research, education and other areas is necessary in order to advance patient care, such support may lead to potential conflicts of interest. Some members of the Alberta Health Services Cancer Care Proton Therapy Guideline Working Group and Guideline Advisory Group are involved in research funded by industry or have other such potential conflicts of interest. However the developers of this guideline are satisfied it was developed in an unbiased manner.

## Guideline Status

This is the current release of the guideline.

## Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the Alberta Health Services Web site .

## Availability of Companion Documents

The following is available:

- Guideline utilization resource unit handbook. Edmonton (Alberta): Alberta Health Services, Cancer Care; 2011 Dec. 5 p. Electronic copies:

Available in Portable Document Format (PDF) from the Alberta Health Services Web site .

In addition, a meeting checklist is provided in the original guideline document for use at multidisciplinary Tumour Board meetings during the patient referral process for out-of-country proton beam radiotherapy treatment.

## Patient Resources

None available

## NGC Status

This NGC summary was completed by ECRI Institute on July 1, 2013. The information was verified by the guideline developer on July 25, 2013.

## Copyright Statement



# Disclaimer

## NGC Disclaimer